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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/590,316

11/28/2006

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EXAMINER

LIU, XUE H

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/590,316	Applicant(s) KAMMERMEIER ET AL.	
	Examiner XUE LIU	Art Unit 1791	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 January 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-38 is/are pending in the application.
- 4a) Of the above claim(s) 34 and 38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-33 and 35-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/28/06 and 8/23/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election without traverse of claims 18-33 and 35-37 in the reply filed on 1/16/09 is acknowledged.
2. Claims 34 and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/16/09.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 18-19 and 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann (US 6465226) in view of Bittner et al. (NPL document Ultrasonic atomization for spray drying: a versatile technique for the preparation of protein loaded biodegradable microspheres).

Regarding claim 18, Zimmermann teaches a process for preparing microspheres comprising an ionically crosslinked polymer, the process comprising: (a) producing liquid aerosol droplets from a solution comprising an ionically crosslinkable polyionic polymer into a gas stream comprising compressed air and the droplets by using a nebulizing nozzle; (b) transferring the gas stream into a gelling solution comprising

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bivalent or trivalent ions, whereby crosslinked polymer microspheres are formed

(abstract, col. 2, lines 65 to col. 3, lines 29, col. 6, lines 38-45, col. 7, lines 28-31).

Zimmermann does not positively characterize the gas stream as continuous. However, it is obvious that the gas stream is continuous since a constant airflow is needed to separate the droplets from the nozzle (abstract, col. 3, lines 8-15). Zimmermann does not teach using an ultrasonic nebulizer for forming the continuous gas stream. However, Bittner et al. teach an ultrasonic atomization method for preparing microspheres by using an ultrasonic atomizer 7 connected to a stream of carrier air 6 to produce liquid aerosol droplets from a solution comprising a polymer into a continuous gas stream 8 (abstract, fig. 1, page 331, lines 1-6). It would have been obvious to one of ordinary skill in the art to provide the ultrasonic nebulizer as taught by Bittner et al. in the process of Zimmermann since Bittner et al. teach that ultrasonic nozzles have the advantage of generating droplets with a relatively uniform size distribution which could lead to more homogeneous size distribution of microspheres (page 326, lines 39-42). In addition, ultrasonic atomizers also permit easy adjustment of particle size by varying the oscillation frequency. Zimmermann does not positively characterize a separating step of the microspheres from the gelling solution. However, it is inherent that the microspheres are separated from the gelling solution since Zimmermann teaches a dwell time of 10-15 minutes of the microspheres in the precipitation bath (col. 3, lines 24-29).

Regarding claim 19, Zimmermann teaches that the ionically crosslinkable polymer is a polyanionic polymer and the gelling solution comprises a polyvalent cation (abstract, col. 4, lines 18-19, col. 6, lines 9-22 and 43-45).

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Regarding claim 21, Zimmermann teaches that the ionically crosslinkable polymer is a polyanionic polymer and the gelling solution comprises di-, multi- or polyvalent cations (col. 4, lines 18-19 and col. 6, lines 38-45).

Regarding claims 22-24, Zimmermann teaches that the polyanionic polymer is alginate (abstract, col. 6, lines 9-21 and col. 7, lines 28-31).

Regarding claim 25, Zimmermann teaches that in step (a), the polyanionic polymer is present in a concentration of less than 5% by weight (col. 2, lines 56-63).

Regarding claims 26-27, Zimmermann teaches that the ion of the gelling solution is a metal cation such as Ba^{2+} and other bivalent cations (col. 6, lines 39-42).

6. Claims 20 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann and Bittner et al. as applied to claim 19 above, and further in view of Lim (US 4,352,883).

Regarding claim 20, Zimmermann does not teach that the polyvalent cation of the gelling solution is selected from the group consisting of poly (allylamine hydrochloride), poly (ethylene imine), poly (diallyldimethylammonium chloride), polyamide-polyamine-epichlorhydrine, chitosan, amino-dextran, and protamine sulfate. However, Lim teaches that the polyvalent cation of the gelling solution is polyethyleneimine (col. 7, lines 59-64). It would have been obvious to one of ordinary skill in the art to select polyethyleneimine as the polyvalent cation in the gelling solution in the method of Zimmermann since Lim teaches that polysaccharide can be (a) gelled to form a shape retaining mass by being exposed to a change in conditions such a ph change or by being exposed to multivalent cations such as Ca^{++} ; and (b) permanently “crosslinked” or

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hardened by polymers containing reactive groups such as amine or imine groups which can react with acidic polysaccharide constituents (col. 2, lines 37-46).

Regarding claim 28, Zimmermann teaches that the ion of the gelling solution is a metal cation such as Ba^{2+} and other bivalent cations. Zimmermann does not positively teach that the metal cation of the gelling solution is Ca^{2+} . However, Lim teaches that Ca^{2+} is used as the metal cation of the gelling solution (col. 2, lines 37-42). It would have been obvious to one of ordinary skill in the art to select Ca^{2+} as the metal cation of the gelling solution in the method of Zimmermann since Lim teaches that Ca^{2+} is a multivalent cation which forms crosslinked polymer microspheres with polysaccharide (col. 2, lines 37-42).

7. Claims 29-30, 32 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann in view of Bittner et al. as applied to claim 18 above, and further in view of Andersson et al. (WO 03/091315).

Regarding claims 29-30 and 36, Zimmermann does not teach that the gelling solution additionally comprises a surfactant present in an amount of from 0.05 to .15% by weight. However, Andersson et al. teach that droplets which form polysaccharide beads are collected in a bath comprised of a liquid having a reduced surface tension by adding a surfactant to the liquid (page 7, line 25- page 8, line 1). It would have been obvious to one of ordinary skill in the art to incorporate the teaching of Andersson et al. in the method of Zimmermann to provide a surfactant in the gelling solution to facilitate movement of the beads in the solution. Andersson et al. do not positively teach the amount of surfactant that is added, however, it would have been obvious to one of ordinary skill in the art to

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select an appropriate amount of surfactant to satisfactorily lower the surface tension of the solution.

Regarding claim 32 and 37, Zimmerman does not positively teach that the temperature of the solution of the ionically crosslinkable polyionic polymer according to step (a) is kept within a temperature of from 25 to 35 deg C. However, Andersson et al. teach the temperature of the polysaccharide solution should be kept low, such as below about 40 deg C (page 5, lines 2-4). It would have been obvious to one of ordinary skill in the art to incorporate the teaching of Andersson et al. in the method of Zimmermann since Andersson et al. teach that keeping the solution at a low temperature avoids formation of lumps (page 5, lines 2-4).

Regarding claim 35, Zimmerman does not teach filtering the microspheres through a screen. However, Andersson et al. teach filtering the beads to a sieve 14 for particle concentration (page 13, line 5 and fig. 1). It would have been obvious to one of ordinary skill in the art to provide the filtering step as taught by Andersson et al. in the method of Zimmermann in order to obtain microspheres with a more uniform size distribution.

8. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman in view of Bittner et al. and Andersson et al. as applied to claim 29 above, and further in view of Lemoine et al. NPL document Preparation and characterization of alginate microspheres containing a model antigen).

Regarding claim 31, Andersson et al. do not positively teach that the surfactant is selected from the group consisting of polyoxyethylene sorbitans and surfactants comprising a block copolymer of ethylene oxide and/or propylene oxide. However,

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Lemoine et al. teach the use of polyoxyethylene sorbitan trioleate as surfactant in the production of alginate microspheres (see section 2.1). It would have been obvious to one of ordinary skill in the art to use polyoxyethylene sorbitan trioleate as surfactant in the method of Zimmermann since Lemoine et al. teach that polyoxyethylene sorbitan trioleate, or Tween 85 produced less heterogeneous and smaller microspheres (table 1 and section 3.1).

9. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmermann in view of Bittner et al. as applied to claim 21 above, and further in view of Vasington et al. (US 5,387,522), Andersson et al. (WO 03/091315) and Lemoine et al. NPL document Preparation and characterization of alginate microspheres containing a model antigen).

Regarding claim 33, Zimmermann teaches that in step (a), the solution comprises about 2 % by weight sodium alginate (col. 2, lines 56-63). Zimmermann does not teach that the solution comprises of from 0.75% to 1.5% by weight of sodium alginate. Zimmermann does not positively teach that the sodium alginate is low viscosity.

However, Vasington et al. teach low viscosity sodium alginates that are used as the polyanionic polymer. Further, Vasington et al. teach that the concentration of the sodium alginates in the mixture should range from about 0.5 to about 1.4%, preferably about 0.6 to 1.2%, most preferably about 0.7-0.9% (col. 5, lines 17-51). It would have been obvious to one of ordinary skill in the art to incorporate the teaching of Vasington et al. in the method of Zimmermann et al. since Vasington et al. teach that low percentage of sodium alginate result in higher porosity of the gel beads to nutrients and other factors (col. 5, line 46-51). Moreover, lowering the viscosity of sodium alginates produces

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smaller microspheres. Zimmermann teaches that the ion of the gelling solution is a metal cation such as Ba^{2+} and other bivalent cations. Zimmermann does not positively teach that the metal cation of the gelling solution is Ca^{2+} . However, Vasington et al. teach that the cation in the gelling solution is Ca^{2+} (col. 6, lines 46-48, col. 7, lines 28-32 and col. 8, lines 42-47). It would have been obvious to one of ordinary skill in the art to use Ca^{2+} as the cation in the gelling solution as taught by Vasington et al. since Vasington et al. teach that Ca^{2+} forms stable calcium alginate gel containing entrapped cells (col. 8k lines 42-47). Zimmermann does not teach that the gelling solution additionally comprises a surfactant present in an amount of from 0.05 to .15% by weight. However, Andersson et al. teach that droplets which form polysaccharide beads are collected in a bath comprised of a liquid having a reduced surface tension by adding a surfactant to the liquid (page 7, line 25- page 8, line 1). It would have been obvious to one of ordinary skill in the art to incorporate the teaching of Andersson et al. in the method of Zimmermann to provide a surfactant in the gelling solution to facilitate movement of the beads in the solution. Andersson et al. do not positively teach the amount of surfactant that is added, however, it would have been obvious to one of ordinary skill in the art to select an appropriate amount of surfactant to satisfactorily lower the surface tension of the solution. Andersson et al. do not positively teach that the surfactant is poly (oxyethylene) 20-sorbitane monolaureate. However, Lemoine et al. teach the use of polyoxyethylene sorbitan trioleate as surfactant in the production of alginate microspheres (see section 2.1). It would have been obvious to one of ordinary skill in the art to use polyoxyethylene sorbitan trioleate as surfactant in the method of Zimmermann since Lemoine et al. teach that polyoxyethylene sorbitan trioleate, or Tween 85 produced less heterogeneous and

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smaller microspheres (table 1 and section 3.1). While Andersson et al. teach the use of polyoxyethylene sorbitan trioleate, as opposed to poly (oxyethylene) 20-sorbitane monolaureate as recited in claim 33. It would have been obvious to one of ordinary skill in the art to substitute polyoxyethylene sorbitan trioleate with poly (oxyethylene) 20-sorbitane monolaureate since both surfactants are structurally similar.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to XUE LIU whose telephone number is (571)270-5522.

The examiner can normally be reached on Monday to Friday 9:30 - 6:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Phillip Tucker can be reached on (571)272-1095. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/X. L./

Examiner, Art Unit 1791

/Philip C Tucker/

Supervisory Patent Examiner, Art Unit 1791